

REMARKS

Status of the Claims

Claim 82 is amended so that "a coding sequence for a biologically active polypeptide operably linked to a nucleotide sequence comprising a 5' leader sequence, wherein said 5' leader sequence consists of SEQ ID NO:16" is now "a coding sequence for a biologically active polypeptide and an operably linked 5' leader sequence consisting of SEQ ID NO:16." The amendment is made to clarify the claim language. Accordingly, no new matter has been introduced by way of the claim amendment.

This claim amendment was not presented earlier as Applicants earnestly believed that the language of claim 82 was clear, and that the claims were directed to patentable subject matter. The amendment to claim 82 is intended to place the claims into condition for allowance or into better condition for appeal. Entry of this amendment is therefore respectfully requested.

Claims 82-24 and 87-94 are pending in the application. In view of the amendments above and the remarks below, Applicants respectfully request reconsideration of the merits of this application. The Examiner's comments in the Office Action are addressed below in the order set forth therein.

Related Patents and Applications

In the interest of maintaining Applicants' duty of disclosure, Applicants wish to explicitly inform the Examiner that pending and co-owned US Patent Application No. 10/794,615, which is cited below in an obviousness-type double patenting rejection, was allowed August 8, 2009. US Patent Application No. 10/794,615 will issue with claims directed toward methods of making monoclonal antibodies in duckweed plant or nodule cultures in which an operably linked 5' leader sequence consisting of SEQ ID NO:16 is recited.

Rejections Under 35 U.S.C. § 103 Should Be Withdrawn

Claims 82-84 and 87-92 remain rejected as obvious over Int'l Patent Application Publication No. WO 99/07210 by Stomp *et al.* in view of Wong *et al.* (1992) *Plant Mol. Biol.* 20:81-93, Buzby *et al.* (1990) *Plant Cell* 2:805-814, and Stiekema *et al.* (1983) *Nucleic Acids Res.* 11:8051-8061.

Likewise, Claims 82-84 and 87-92 remain rejected as obvious over Stomp *et al.*, *supra*, in view of Wong *et al.*, *supra*; Buzby *et al.*, *supra*, US Patent No. 5,460,952 to Yu *et al.*, Park *et al.* (1997) *J. Biol. Chem.* 272:6876-6881, and Stickema *et al.*, *supra*.

In support of the rejections, the Examiner states that Buzby *et al.* is cited only to teach a 5' leader sequence comprising SEQ ID NO:16 and that Wong *et al.* is cited to teach that one of skill in the art understands that a 5' leader sequence of ribulose-1,5-bisphosphate carboxylase (rbcS), including one from duckweed, can enhance protein expression. The rejections are respectfully traversed.

As in previous responses, Applicants address the rejections together below because each relies upon common, principal citations (*i.e.*, Stomp *et al.*, Buzby *et al.*, and Wong *et al.*). In contrast to the cited references, Applicants were the first to discover that SEQ ID NO:16 alone can enhance heterologous, biologically active polypeptide expression in duckweed. Claim 82 is amended above to clarify that the 5' leader sequence consists of SEQ ID NO:16.

Establishing a *prima facie* case of obviousness requires an assessment of the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1 (1966), which provides a framework for applying the statutory language of § 103 (*i.e.*, the "Graham Factors"). Under the Graham Factors, an examiner must:

1. Determine the scope and content of the prior art;
2. Ascertain the differences between the prior art and the claims at issue;
3. Resolve the level of ordinary skill in the pertinent art; and
4. Consider any relevant secondary considerations.

Recently, the Supreme Court identified seven (7) rationales for use in supporting obviousness determinations, which are consistent with *Graham*. MPEP § 2143. Regardless of the applied rationale, prior art "can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success." MPEP § 2143.02 I. The reasonable expectation of success is not required to be absolute (MPEP § 2143.02 II.), but must be determined at the time the invention was made (MPEP § 2143.02 III.). Thus, "evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness." MPEP § 2143.02.

The claimed invention is directed toward stably transformed duckweed plant or nodule cultures where the 5' leader sequence consists of SEQ ID NO:16. As shown throughout the application, SEQ ID NO:16 not only substantially increases production of recombinant polypeptides, but also reduces the culture time needed for the plant or nodule cultures to produce such levels of polypeptides. Neither the polypeptide levels nor the growth times disclosed in the application can be predicted from the cited references.

With respect to Stomp *et al.*, Applicants again briefly reiterate comments from previous responses. Stomp *et al.* provide only general teachings regarding methods of modifying nucleic acid molecules to enhance expression in duckweed of biologically active polypeptides. As the Examiner previously acknowledged, Stomp *et al.* does not contemplate or disclose using SEQ ID NO:16 alone to enhance expression of biologically active polypeptides.

Buzby *et al.* and Wong *et al.* are cited as bridging the gaps between Stomp *et al.* and the pending claims by guiding one of skill in the art to any and all ribulose-1,5-bisphosphate carboxylase (rbcS) 5' leader sequences, including SEQ ID NO:16. As amended, Claim 82 limits the 5' leader sequence to only SEQ ID NO:16, thereby excluding the use of the whole rbcS promoter region of Buzby *et al.* Neither Buzby *et al.* nor Wong *et al.* direct one of skill in the art specifically to the sub-sequence of SEQ ID NO:16. Thus, one of skill in the art had no reason to specifically isolate SEQ ID NO:16 from the whole rbcS promoter region of Buzby *et al.*

Stickema *et al.*, Yu *et al.*, and Park *et al.* are cited as bridging the gaps between Stomp *et al.* and the pending claims by guiding one of skill in the art to signal or transit peptides such as the rice α -amylase signal peptide including the one set forth in SEQ ID NO:6. Amended Claim 82, however, has no requirement for a transit/signal peptide sequence to enhance translation. Instead, it relies on the use of the 5' leader sequence as set forth in SEQ ID NO:16. As noted above, SEQ ID NO:16 was found to significantly enhance heterologous protein production in duckweed while decreasing production time. Because no combination of Stomp *et al.*, Buzby *et al.*, Wong *et al.*, Stickema *et al.*, Yu *et al.* and Park *et al.* contemplates or discloses SEQ ID NO:16 alone operably linked to a heterologous promoter, they cannot render obvious Claim 82 and the claims that depend therefrom. In view of the amendment above and foregoing remarks, as well as for all of the reasons of record, Applicants respectfully request reconsideration and withdrawal of the obviousness rejections.

Non-Statutory Obviousness-Type Double Patenting Rejections

Claims 82-84 and 87 remain rejected under the judicially created doctrine of obviousness-type double patenting as patentably indistinct from Claims 16-17 of US Patent No. 6,815,184 to Stomp *et al.* (hereinafter Stomp II) in view of Buzby *et al.*, *supra*, and Wong *et al.*, *supra*. This rejection is respectfully traversed.

The pending claims are directed toward stably transformed duckweed plant and nodule cultures where the 5' leader sequence consists of SEQ ID NO:16. Stomp II, however, does not contemplate or disclose the use of this 5' leader sequence. As noted above, Buzby *et al.* and Wong *et al.* do not contemplate or disclose a 5' leader sequence "consisting of" SEQ ID NO:16. Given the teachings of each reference, one of skill in the art had no expectation of success that SEQ ID NO:16 alone could be used in duckweed to significantly enhance heterologous protein production while decreasing production time. In view of the amendment above and foregoing remarks, as well as for all of the reasons of record, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 82-84 and 87-94 remain rejected under the judicially created doctrine of obviousness-type double patenting as patentably indistinct from Claims 3, 8-10, 23, and 26-29 of commonly owned US Patent Application No. 10/794,615 by Dickey *et al.* As noted above, a Notice of Allowance has now been issued for US Patent Application No. 10/794,615. At which time allowable subject matter is agreed upon in the case of the present application, Applicants will timely file the required terminal disclaimer and appropriate fee to address this double-patenting rejection.

Claims 82-84 and 87 remain rejected under the judicially created doctrine of obviousness-type double patenting as patentably indistinct from Claims 1-25 of US Patent Application No. 11/778,480 by Stomp *et al.* (Stomp III) in view of Wong *et al.*, *supra* and Buzby *et al.*, *supra*. As noted in previous responses, Applicants believe this rejection should be a provisional rejection. As such, no response is required at this time. However, this application and the '480 application are commonly owned. Applicants therefore will consider the filing of a terminal disclaimer should allowable subject matter be agreed upon in either case and should the Examiner maintain the double-patenting rejection over the '480 application.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully submit that the rejection of claims 82-84 and 87-94 should be withdrawn. Accordingly, Applicants submit that this application is in condition for allowance. Early notice to this effect is solicited.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefor (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

/leslie t. henry/

Leslie T. Henry
Registration No. 45,714

Customer No. 00826 ALSTON & BIRD LLP Bank of America Plaza 101 South Tryon Street, Suite 4000 Charlotte, NC 28280-4000 Tel Raleigh Office (919) 862-2200 Fax Raleigh Office (919) 862-2260	ELECTRONICALLY FILED USING THE EFS-WEB ELECTRONIC FILING SYSTEM OF THE UNITED STATES PATENT & TRADEMARK OFFICE ON OCTOBER 19, 2009.
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